REMARKS

Claims

Claims 13, 15, 21, 22, 26, 30, 31, 33, 35 and 36 are currently under examination pursuant to the restriction requirement mailed August 24, 2007 and May 28, 2009.

Claims 1–12 and 16 have been withdrawn from consideration pursuant to the aforementioned restriction and election requirements.

Claims 14, 17–19, 23, 24 and 34 were previously cancelled. Claims 20, 25, 27–29 and 32 are hereby cancelled without prejudice or disclaimer.

Claim amendments

Claim 13 has been amended as per the Examiner's suggestion. Claims 20, 25 and 27–29 are cancelled without prejudice or disclaimer. No new matter is recited. Entry thereof is earnestly requested.

Claim objections

The Examiner is thanked for her careful review of the claims. The foregoing amendments render the objection claims 13 and 22 moot. Withdrawal of the objection is respectfully requested.

Rejections under §102(b)

The contention that the instant claims are anticipated by Fischer et al. (*Journal of Allergy and Clinical Immunology*, 1996) is respectfully traversed.

Fischer teaches decapeptide sequence of Phl p 4 containing ten amino acid residues (IVALPXGMLK) of the N-terminal region of Phl p 4. See, Fig. 5 and the description thereof at page 194 of Fischer et al. The polypeptide by Fischer does not show any homology to the Phl p 4 amino acid sequences of SEQ ID NO: 2, 4 and 6. For example, Lipman-Pearson Alignment analysis and DotPlot analysis with LASERGENE (DNASTAR) merely showed single Phl p 4 regions with sequence identities in three positions. Such low values do not indicate homology but random identities. See Exhibit A (SIM+LALNVIEW analysis).

As such, Applicants assert that Fischer fails to teach or suggest the polypeptides of the present invention, for example, a polypeptides which comprise the sequences set forth in SEQ ID NO: 2, SEQ ID NO: 4, or SEQ ID NO: 6, or a variant of the sequence set forth in SEQ ID NO: 2, with the amino acid variations set forth in clones 1–11. Moreover, the cited reference fails to disclose the structural elements of the claimed fragments, comprising, for example,

50–350 amino acid residues. See, amended claim 21. Absent such, the reference cannot anticipate what is claimed herein. Withdrawal of the rejection is respectfully requested.

With respect to Suck et al. (*Clinical & Experimental Allergy*, 2000), Applicants submit that the reference pertains to Phl p 13, another allergen of *Phleum pretense*. With respect to the disclosure in Fahlbusch et al. (*Clinical & Experimental Allergy*, 1998) and the §102(b) rejection based thereon, the Examiner's allegations are respectfully traversed. Based on the Examiner's rationale at pages 17–18 of the Office Action, it appears that this rejection is based on the cited references' disclosure of the term Phl p 4 polypeptide. The Examiner is alleging that the references' teaching of Phl p1 protein creates a presumption of structural identity. This contention lacks scientific merit. To this end, a search with the term "*Phleum pretense* 'Phl p 1'" in NCBI identifies at least 5 hits, of which 4 accession numbers are directed to Phl p1 (or Phl p I) polypeptides. Three accession numbers relate to polypeptides that are 262-263 amino acids. One accession number relates to a shorter sequence, which was not further analyzed (accession No.: CAG24374; a protein of 240 amino acids). Multiple sequence alignment of these sequences using CLUSTAL (program freely available via EXPASY) reveals three variant sequences. See the enclosed Exhibit B. Therefore, at least three other sequences are recognized by the same name, i.e., Phl p1. More importantly, **none of the identified sequences** met the structural features of the instantly claimed polypeptides (i.e., length of ~500 amino acid residues). As such, the polypeptides of the instant application are novel over what is taught by the prior art.

It is by now well-established that "a claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." See MPEP §2131 and further corroborated by the Fed. Circuit's decision in *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). With respect to inherency, the Courts have established that "the extrinsic evidence 'must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient.'" *In re Robertson*, 169 F.3d 743, 745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999). Inasmuch as the cited Suck et al. and Fahlbush et al. say nothing about Phl p 4 polypeptide sequences and the art (or the Examiner) has not established that the Phl p 4 polypeptide disclosed therein necessarily comprises the sequences recited herein, the rejection is without legal merit.

With respect to the PTO's contention that sequences need not be provided, the controlling case law dictates that for anticipation, "the identical invention must be shown in as

complete detail as is contained in the ... claim." *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989). The Office Action fails to establish that the polypeptides disclosed in the aforementioned references contain the **complete** Phl p 4 polypeptide sequence as presently claimed. To this end, the enclosed Exhibit B unequivocally demonstrates that it cannot be ascertained whether the references teach a sequence that is completely identical to what is claimed in the present application. More importantly, it is clear to those skilled in the art that none of the cited references of Suck et al. and Fahlbusch et al. provide "a complete detail" (i.e., the polypeptide sequence) of the claimed invention. As such, an inherency rejection under §102/§103 is not supported and should be withdrawn. See MPEP §2112.

Moreover, the Examiner has given no basis for alleging that it would be "reasonable" to assume that the references' products are the same as those claimed herein. See *In re Best* 562 F.2d 1252, 1255 n.4, 195 USPQ 430, 433 n.4 (CCPA 1977). If anything, the record summarized above shows such as assumption to be unreasonable. Thus, the burden remains on th Examiner. Withdrawal of the rejection is respectfully requested.

Claims directed to recombinant polypeptides

In view of Applicants' own disclosure, for example, Fig. 4 of the instant specification, it is clear that the recombinant polypeptides of the instant invention are different and thus novel over the natural Phl p 4 polypeptides. Therein, it is expressly disclosed that nPhl p 4 has a higher molecular weight than r Phl 4 of the instant invention. Favorable reconsideration is respectfully requested.

Inventive step

A combination of the aforementioned Fischer et al., Suck et al., and Fahlsburg et al. also fails to render obvious the claimed subject matter.

An embodiment of the present invention pertains to the preparation of recombinant Phl p 4 and hypoallergenic variants and fragments thereof for therapy and diagnostics. The advantages of recombinant proteins over proteins extracted and purified from natural sources are the much higher purity, cheaper preparation and a higher yield and a stable production of a defined protein instead of a mixture of several isoforms and contaminations with other proteins and compounds, leading to a higher yield. Although several peptide fragments of group 4 grass pollen allergens were known since a long time (see, pages 2–4 of the specification), the sequences of these allergens were not elucidated and such sequences were not available at the

time the present application was filed. Obviously the previous attempts were not successful because the the N-terminal amino acid sequence could not be determined. The documents of the International Search Report labeled by an "X" may broadly describe biochemical and immunological properties of *Phleum pretense* allergens, but not the DNA or amino acid sequence thereof. To this end, Suck et al. (*Clin Exp. Allergy* 30, 2000, 32-332) discloses the sequence of Phl p 13, another allergen of *Phleum pratense*.

The previously failed attempts of other scientists to determine the sequence are described in the chapter "background of the invention," their own work and results are disclosed in the chapter "description of the invention." The sequencing of the first 69 amino acids (N-terminus of the allergen) presented an unforeseeable problem. This part of the protein was not accessible to DNA sequencing and had to determined directly and the respective DNA sequence was deduced from this amino acid sequence leading to the "hybrid" sequences 1, 3 and 5 (see specification and the notes to SEQ ID NOs: 1, 3 and 5 in the sequence protocol). The cloning strategy and method is described in detail in Nandy et al. 2005 and the attached posters (see attachments). These documents show that the performed cloning strategy and method was new and inventive and it was not obvious for a person skilled in the art that this method would lead to a successful cloning of Phl p 4. This was a new and inventive approach that was not disclosed or suggested by the state of the art. A further evidence fort he presence of an inventive step is he fact that die elucidation of the coding DNA sequence of Phl p 4 was tried intensively but not successful since the end of the 80s by several scientific groups. Many peptide fragments published e.g. in Fisher et al. are the results of such trials. These fragments neither lead to the elucidation of the DNA or amino acid sequence of Phl p 4 nor to the elucidation of the DNA or amino acid sequence of other group 4 allergens. No scientist would be satisfied with the publication fragments if the full-length sequence would be obtainable by standard technology. Even in 2003 Andersson and Lindholm acknowledge in their review article (see attachments, page 92, right column) that "despite considerable efforts, cloning of a group 4 grass pollen allergen has so far not been reported."

The standard methods being used by a person skilled in the art, like the use of degenerated primers based on the N-terminal peptide sequence, did not lead to the successful cloning of Phl p 4, even when repeated several times. Also the sequence of Phl p 13 according to Suck et al. is based on standard techniques and was not successful in the case of Phl p 4. Obviously, the other scientific groups also tried such standard techniques and were not successful. Thus, the Phl p 4 sequence was not determined and published before the priority date of the present application. Therefore, the cited documents do not give a single hint or do

not lead to or teach the inventive cloning strategy or recombinant Phl p 4. The inventive DNA sequence of Phl p 4 presents the first DNA sequence of a group 4 allergen ever. Before the elucidation of the Phl p 4 DNA sequence and the availability of recombinant Phl p 4 for the use for specific immunotherapy Phl p 4 had to be isolated from grass pollen with all disadvantages described above. Using the methods of the present invention, it can be produced recombinantly in large amounts and in a simple way.

Furthermore, the claimed polypeptides clearly differ from Phl p 4 purified from natural sources as there are clear structural differences between protein allergens isolated from natural sources and isolated recombinant allergens. Recombinantly prepared proteins have several advantages over protein preparations which are obtained by extraction and purification from natural sources. Recombinant proteins have a much higher purity with respect to the target protein than protein preparations obtained by extraction and purification from natural sources. The impurity of allergen preparations obtained by extraction and purification from natural sources is for example disclosed in Hoffman on page 602, table 1 (*J Allergy Clin. Immunol.* 75(5):599-605, 1985). Therein, cross-contaminations by other allergens and contaminations by faecal and proteolytic compounds were shown. These contaminations are very critical for the stability and safety of the product and therefore for its potential use in therapy and diagnosis. This difference in purity is a clear structural difference between protein allergens isolated from natural sources and isolated recombinant allergens. Besides the impurity also the low yield is a critical issue for allergen preparations received by extraction and purification form natural sources.

Favorable reconsideration is respectfully requested.

Rejection under 35 U.S.C. §112, ¶1

Claims 15, 20–22, 25–32 and 35–36 are rejected under this section for allegedly failing to comply with the written description and/or enablement requirements. This contention is respectfully traversed.

At the outset, the rejection is rendered moot with respect to claims directed to vaccines. Applicants' amendment of the claims is not to be construed with acquiescence to this or any other ground of rejection.

The following comments are provided to rebut the Examiner's contention that the claimed polypeptide fragments and pharmaceutical compositions thereof lack adequate written description and/or enablement.

Written description rejection

(a) Polypeptide fragments

Applicant asserts that the claims are in compliance with the PTO's new *Written Description Guidelines*. See for example, Example 5 beginning on Page 17 of the *Training Materials* (Rev. 1, March 25, 2008). Therein, the Guidelines examine an exemplary specifications' ability to satisfy the written description requirements for a claim directed to partial protein structure. It is stated that the exemplary specification discloses a working example in which Protein A was isolated from human urine. This is analogous to Applicants' disclosure of isolation of a recombinant Phl p4 clone 1 (variant of SEQ ID NO: 2), which can be recombinantly prepared. It is further described that Protein A is a 22 kDa protein that binds to and activates Protein X. This situation is analogous to Applicants' disclosure of rPhl p 4 variants having the sequences set forth in the claims, or fragments thereof, wherein each of said rPhl p 4 polypeptides or the fragments thereof are immunogenic and induce immunomodulatory T-cell responses in a host.

With respect to methods of making and using the partial protein sequences, the exemplary specification describes a process for isolating Protein A from human urine, wherein there is further provided data showing that Protein A so isolated binds to and activates Protein X. This is identical to the disclosure in Applicants' specification regarding the structure/activity of two rPhl p 4 fragments of 1–200 a.a. and 185–500 a.a. See the disclosure in Fig. 4 and the description thereof at page 16, lines 15–28 of the originally filed specification. However, in contrast to Applicants' disclosure, the exemplary specification only discloses a 10 amino acid sequence from the N-terminus of Protein A (identified as SEQ ID NO: 1), while the complete sequence of Protein A is **not** disclosed. The exemplary claim is as follows:

> **Claim 1.** An isolated protein comprising Protein A, wherein said Protein A includes the amino acid sequence of SEQ ID NO: 1 in the N-terminal portion of the protein, and has the same ability to bind to and activate Protein X as Protein A from human urine, and wherein said Protein A is purified by subjecting a crude protein recovered from a dialyzed concentrate of human urine to affinity chromatography on a column of immobilized Protein X, and elutes from a reversed-phase HPLC column as a single peak in a fraction corresponding to about 31% acetonitrile and shows a molecular weight of about 22 kDa when measured by SDS-PAGE under reducing conditions.

The Guidelines explicitly state that the exemplary specification *satisfies* the written description requirement of §112, ¶1 with respect to the full scope of claim 1. In the discussion section at page 18, it is stated that even though the exemplary specification **fails to disclose the complete structure of Protein A** [and] **also fails to disclose any art-recognized correlation between the structure of the claimed protein and its function of binding and activating Protein X** the disclosure of partial structure and other relevant identifying characteristics of the

protein, along with a working example for the isolation of the partial protein imparts adequate written description. The Guidelines further state that, "**those of ordinary skill in the art of isolating proteins would recognize the inventor to have been in possession of the claimed protein at the time of filing based on these identifying characteristics and the disclosed isolation method** (emphasis added)."

Likewise, in the instant application, all the relevant characteristics of the rPhl p 1 variants and fragments thereof are provided in the specification. For example, the sequences of clones 1–12 of SEQ ID NO: 2 can at once be obtained by performing amino acid substitutions and/or insertions at the recited positions of the native sequence of SEQ ID NO: 2. The variants thus produced can be assayed for immunogenic and T-cell reactive activity using the methods described in the Examples (e.g., binding to monoclonal antibodies). Similarly, N-terminal fragments of each of the variants comprising the first 200 amino acids or C-terminal fragments of each of the variants comprising the last 316 amino acids (i.e., amino acids 185-500) can be generated using the techniques described in the Examples. Thus the structural information of six fragment sequences of the native allergens (i.e., N-terminal and C-terminal fragments of SEQ ID NOs: 2, 4, and 6) and 24 fragments from variant allergens (i.e., N-terminal and C-terminal fragments of clones 1–12 of SEQ ID NO: 2) are explicitly taught by the instant application. Other representative examples of such fragment sequences, for example, P1-P6 (SEQ ID NOs: 27-32) obtained from the amino acid sequencing of the purified and fragmented Phl p 4 allergens are additionally described in the instant application.

The PTO's contention that the disclosure of specific examples of rPhl p 4 polypeptide sequences, i.e., SEQ ID NOs: 2, 4, or 6, fails to provide adequate written description for the genus of the claimed polypeptides is respectfully traversed. Firstly, this is different from *University of California v. Lilly*, 964 F.2d 1128 (Fed. Cir. 1997) or *University of Rochester v. Searle*, 358 F.3d 1303 (Fed. Cir. 2004) where functional language was involved with insufficient structural details available for a chemical compound. These facts here are similar to those in *Capon v. Eshhar*, 76 USPQ2d 1078, 1082 (Fed. Cir. 2005) and *Falkner v. Inglis,* 448 F.3d 1357 (Fed.Cir. 2006). In these cases, the court held that even where there are no examples within the scope of a claimed genus, a written description exists where the elements of the members of the genus are known. Here, based on the complete disclosed rPhl p 4 sequences (e.g., SEQ ID NOs: 2, 4, and 6), variant sequences are *also* comprehensible without explicitly listing each and every sequence. The specification provides representative examples of polypeptides, for example, clones 1–12 of SEQ ID NO: 2. Furthermore, in view of the detailed level of knowledge in molecular biology and the sophisticated tools available to the skilled worker, *any* fragment

sequence which meets the claimed structural (i.e., amino acid sequence) can be can be generated. For example, the sequences can be generated using recombinant preparative methods or enzymatic digestion of the native sequence. Additionally, functional features (e.g., immunogenic activity) of these fragments and variants can be routinely tested. Explicit description is therefore not necessary.

Applicants bring to the Examiner's attention Example 12 at page 43 of the *Training Materials* (Rev. 1, March 25, 2008). The exemplary specification discloses a messenger RNA (mRNA) sequence that encodes newly discovered growth factor (NDG): SEQ ID NO: 1 (which is similar to Applicants' rPhl p 4 polypeptide). The specification states that the invention *includes* antisense oligonucleotides that inhibit the production of NDG, but does not disclose the sequences of any antisense oligonucleotides (emphasis added). The antisense oligonucleotides are analogous to Applicants' rPhl p 4 fragments.

Representative claim of the Example reads as follows:

> **Claim 1.** An antisense oligonucleotide complementary to all or a portion of a messenger RNA having SEQ ID NO: 1 and encoding NDG, wherein said antisense oligonucleotide inhibits the production of NDG.

The guidelines state that claim 1 satisfies the statutory requirements set forth under §112, ¶1, even though the minimal structural requirement (i.e., length or sequence) of such antisense molecules **is not expressly disclosed** by the exemplary specification. To this end, in the paragraph bridging pages 44 and 45 of the *Guidelines*, it is explicitly stated:

> The specification does not disclose the full or partial structures of any other species within the genus of claim 1. However, the structure of all possible antisense oligonucleotides that are complementary to NDG mRNA can be predicted from the full-length complement of SEQ ID NO: 1. Even though all of the oligonucleotides that are complementary to NDG mRNA will not have antisense function, there are certain art-recognized correlations between the antisense oligonucleotide's function and the structure of the target mRNA that would aid the selection of those fragments having antisense activity (Emphasis added).

Likewise, in the instant application, insofar as the complete structures of the claimed polypeptides and variants thereof are provided by the originally-filed specification, the structure of all possible fragment polypeptides can be predicted from the full-length putative sequences. This applies equally well to the claimed fragment sequences of 200 amino acids or 316 amino acids of SEQ ID NO: 2. To hold the subject matter of the present claims as lacking adequate written description would be contrary to the agency's own published guidelines. Withdrawal of the rejection is respectfully requested.

Pharmaceutical compositions

The Office Action alleges that the pharmaceutical compositions are not adequately described. This contention is respectfully traversed. The disclosure bridging page 18, line 5 to page 19, line 5 of the originally-filed specification provides more than adequate written description of pharmaceutical compositions comprising r Phl p 4 polypeptides. For example, the specification teaches that pharmaceutical compositions comprise a polypeptide according to the invention as active ingredients, which is brought here into a suitable dosage form together with at least one solid, liquid and/or semi-liquid excipient or adjuvant and optionally in combination with one or more further active ingredients. The specification further teaches that particularly suitable adjuvants are immunostimulatory DNA or oligonucleotides having CpG motives, lubricants, preservatives, stabilisers and/or wetting agents, emulsifiers, salts for modifying the osmotic pressure, buffer substances, etc. This demonstrates *possession* of the claimed subject matter. As such, the USPTO's contentions are without merit.

Enablement

Claims directed to polypeptide fragments

Applicants' claims are now directed to polypeptide molecules and fragments thereof comprising specific sequences. Variants of the claimed molecules, comprising, for example, the amino acid variations at the recited position in the polypeptide sequence of SEQ ID NO:2 are further disclosed. The detailed disclosure contained in Applicants' specification (as substantiated by the disclosure of three polypeptide sequences and 11 other clonal variants) provides a detailed description of the structure/activity of the claimed variant sequences and fragments. See also, the sequence listing page and the tables. The biological activities of such polypeptide molecules, for example, with respect to their reactivity to IgE molecules, are further discussed in the Examples section. See, the disclosure in Fig. 5 and the description thereof at page 6 of the present application. As such, the specification provides an enabling disclosure of the claimed polypeptide fragments, and immunogenic activity thereof. The entire genus of Applicants' claimed polypeptide fragments could be routinely generated, for example, using the recombinant preparative schemes described by the present specification. Such fragments could be further tested, for example, with respect to binding to monoclonal antibodies (Fig. 4) and/or IgE reactivity (Fig. 5). The whole process would constitute nothing beyond what is routine in the art.

Claims directed to the pharmaceutical composition/vaccines

In the paragraphs bridging pages 11 and 12, the Office Action alleges that the pharmaceutical compositions and/or vaccines of the present invention are non-enabled. This contention is respectfully traversed.

Applicants' specification, coupled with a skilled worker's knowledge, provides more than adequate guidance on how to make the claimed polypeptide molecules and use pharmaceutical compositions and medicaments comprising such polypeptides for immunotherapy. The specification provides both general and specific guidance regarding the specific epitopes in allergens and how such could be manipulated for reliable hyposensitisation. See, for example, the disclosure contained in the paragraphs bridging [0031]–[033] of the published specification and the reference article by Schramm et al., 1999, *J. Immunol.* 162: 2406-2414. With respect to DNA vaccines, the specification explicitly teaches that "experimental evidence of allergen-specific influencing of the immune response has been furnished in rodents by injection of allergen-encoding DNA (Hsu et al., 1996, *Nature Medicine* 2 (5): 540-544)." Furthermore, the specification of the present application discloses specific immunotherapy or desensitization as therapeutic field for especially recombinant allergen proteins with higher purity and therefore reduced side effects than allergen proteins isolated from natural sources which are always mixtures of compounds. To this end, the specification discloses strategies to minimize the risks of side effects with the development of T-cell reactive fragments with reduced or no IgE-reactivity leading to hypoallergenic peptides (see, the section bridging paragraphs [0063]–[0067] of the published specification). The screening for T-cell and IgE epitopes were common knowledge at the priority date of the present application. Thus, a person skilled in the art would have been able to identify T-cell and IgE epitopes and produce hypoallergenic peptides. Nevertheless, also the classic approaches of specific immunotherapy and desensitization were applicable as a skilled person would have known the pharmaceutical effects and also the side effects and risks of an allergen protein administered to a patient and would have followed clinical recommendation protocols for specific immunotherapy and desensitization.

In relation to an enabling disclosure on the utilization of grass pollen allergen polypeptides in treatment of subjects, the specification provides a detailed disclosure for the design, synthesis and use of recombinant allergen extracts with reduced IgE reactivity. See, for example, the disclosure contained in Figs. 4 and 5. To this end, the Examiner is also courteously invited to review the disclosure contained in Focke et al. (Focke et al., *FASEB Journal*, 15, 2042-44, 2001), a copy of which is enclosed herewith. As evidenced by the disclosure in the "Principle Findings" section of Focke and the immunoglobulin reactivity data provided in

Table 1, it is respectfully submitted that as of the filing date of the present application, the instantly claimed grass pollen allegens could be routinely manipulated and utilized as pharmaceutical preparations in a manner recited in the claims.

Thus it is respectfully submitted that the specification provides an enabling disclosure on the claimed allergenic properties of the recombinant, *Phleum pratense* allergen polypeptides of the instant invention. Therefore, the specification's express teaching that the claimed compounds are pharmaceutically useful is clearly credible as required. The PTO's contentions regarding non-enablement are especially weak in view of the detailed disclosure contained in Applicants' own specification and the state of the art before the earliest filing date of the instant application. Withdrawal of the rejection is respectfully requested.

To support the contention of non-enablement, the Office Action cites Tarzi (*Expert Opinion in Biol. Ther.*, 2003) to allege that whole allergen immunotherapy is unpredictable. However, even Tarzi discloses the therapy of allergic diseases with specific immunotherapy or desensitization in general being effective and successfully applied for many years. See, the last paragraph at page 617 of the cited reference. Moreover, in Gefter et al. (USP 6,795,234) discloses that the risk of systemic reactions like anaphylactic shock can be effectively minimized in individuals via specific immunotherapy, wherein pharmaceutical compositions comprising allergen polypeptides and/or vaccines comprising DNA sequences which encode such polypeptide allergens are utilized. See, the complete third and fourth paragraphs in the "BACKGROUND OF THE INETNION" (especially, col. 1, lines 26–45) of Gefter's USP '234. As such, the PTO's contentions of non-enablement, based on the disclosure contained in Tarzi is without merit.

The final Office Action at page 6 alleges that it would "take undue trials and errors to practice the claimed invention." These allegations, however, do not present any evidence to doubt the objective enablement of Appellants' disclosure. As clearly and succinctly stated by the court in *In re Marzocchi*, 169 USPQ 367, 369 (CCPA 1971):

> As a matter of Patent Office practice, then a specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented **must** be taken in compliance with the enabling requirement of the first paragraph of §112, **unless** there is reason to doubt the objective truth of statements contained therein relied on for enabling support. (emphasis in original)

Furthermore, as stated in *Marzocchi*, at 370, the PTO must have adequate support (evidence or reasoning) for its challenge to the credibility of Appellants' statements of

enablement. Thus, in the absence of evidence which demonstrates otherwise, the claims must be taken to satisfy the requirements of 35 U.S.C. § 112, ¶1.

Working examples are not required to establish enablement. As stated by the court *Marzocchi*, at page 369:

> The first paragraph of §112 requires nothing more than objective enablement. How such a teaching is set forth, either by the use of illustrative examples or by broad terminology, is of no importance.

The assertion of undue experimentation in the rejection is merely conclusory. Further, as discussed above, the specification provides more than sufficient guidance to make and use the claimed medicaments and/or pharmaceutical compositions using no more than routine experimentation. Finally, a high level of skill does not establish that one skilled in the art would have reasons to doubt the veracity of the statements in Appellants' specification with respect to the use of the claimed composition in the diagnosis, treatment, and/or prevention of the claimed conditions.

Based on the aforementioned remarks and arguments, further in view of the amendments presented herein, it is respectfully submitted that Applicants' specification provides an enabling disclosure of what is claimed by the present invention. Withdrawal of the rejection under 35 U.S.C. §112, ¶1, is respectfully requested.

In view of the above remarks, favorable reconsideration is courteously requested. If there are any remaining issues which could be expedited by a telephone conference, the Examiner is courteously invited to telephone counsel at the number indicated below.

The Commissioner is hereby authorized to charge any fees associated with this response to Deposit Account No. 13-3402.

Respectfully submitted,

/Sagun KC/

Sagun KC, Reg. No. L0510
For Applicant(s)

/Anthony J. Zelano/

Anthony J. Zelano, Reg. No. 27,969
Attorney for Applicant(s)

MILLEN, WHITE, ZELANO
& BRANIGAN, P.C.
Arlington Courthouse Plaza 1, Suite 1400
2200 Clarendon Boulevard
Arlington, Virginia 22201
Telephone: (703) 243-6333
Facsimile: (703) 243-6410

Attorney Docket No.: MERCK-2966

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